

Sub 1



R¹ to R⁷ are independently selected from H, optionally substituted C₁₋₆ alkyl, C₂₋₆ alkenyl and C₂₋₆ alkynyl, optionally substituted aryl or heteroaryl, OH, halogen, CN, OR¹², SR¹², COR¹², COOR¹², SOR¹², SO₂R¹², NR¹³R¹⁴, CONR¹³R¹⁴, SO₂NR¹³R¹⁴, where R¹³ and R¹⁴ are independently selected from H and C₁₋₃ alkyl and R¹² represents C₁₋₆ alkyl; two of R¹ to R⁷, together with the atoms connecting them, each may form a 3- to 6-membered ring system, which ring system may contain one or more heteroatoms; R¹ and R² and/or R³ and R⁴ and/or R⁵ and R⁶ may be replaced by an optionally substituted alkylidene group or =O; and two of R¹ to R⁷ which are positioned at adjacent carbon atoms may each be replaced by a C-C bond;

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X is selected from COOM and groups which can be converted into COOM under physiological conditions, M being selected from H and pharmaceutically acceptable cations;

A² is $(-CR^{10}R^{11})_m$, where R¹⁰ and R¹¹ are independently selected from H, C₁₋₂ alkyl and halogen; where for m ≥ 2 the groups R¹⁰ and R¹¹ may be different in each group, a group -O- or -S- may be positioned between two adjacent groups -CR¹⁰R¹¹-, and two groups selected from R¹⁰ and R¹¹ at adjacent C atoms may be replaced by a C-C bond; and wherein one of R¹⁰ and R¹¹ may be combined with one of R¹ to R⁹ to form a 5- to 7-membered ring structure; and m is 1, 2, 3, or 4;

Z is selected from Y₃C-O-, Y₂C=CR¹⁵- and Y₂C=N-O-, where R¹⁵ is selected from H, C₁₋₃ alkyl or halogen and the groups Y are independently selected from optionally substituted C₆₋₁₂ aryl and optionally substituted C₂₋₅ heteroaryl having up to three heteroatoms independently selected from N, O and S, and the groups Y may be linked by a covalent bond or by groups between atoms belonging to different groups Y, said groups selected from -O-, -S-, -NH-, -O-, -CH=CH-, -CH=N-, -CH₂- and -CH₂CH₂-;

as well as the individual stereoisomers of these compounds.

32. The compound of claim 31, wherein R⁷ is hydrogen and R¹ to R⁶ are independently selected from hydrogen, optionally substituted C₁₋₃ alkyl, halogen, OH, CN, optionally substituted phenyl and optionally substituted heteroaryl having 5 to 10 ring members and one or two heteroatoms selected from O, N and S.

3 ² 33. The compound of claim 32, wherein R¹ to R⁶ are independently selected from hydrogen, C₁₋₃ alkyl and phenyl.

4 ~~34~~. The compound of claim ~~33~~³, wherein all of R^1 to R^7 represent hydrogen.

5 ~~35~~. The compound of claim ~~31~~¹, wherein A^1 is $(-CR^8R^9-)_n$, R^8 and R^9 are independently selected from H and C_{1-3} alkyl and n has a value of 1, 2 or 3.

6 ~~36~~. The compound of claim ~~35~~⁵, wherein R^8 and R^9 are each hydrogen and n has a value of 1 or 2.

7 ~~37~~. The compound of claim ~~34~~⁴, wherein X is COOM, with M = H, Na, K, NH_4 , $Ca_{0.5}$ or $Mg_{0.5}$.

8 ~~38~~. The compound of claim ~~37~~⁷, wherein X is selected from H and Na.

9 ~~39~~. The compound of claim ~~31~~¹, wherein R^{10} and R^{11} are independently selected from H and C_{1-2} alkyl and m is 2 or 3.

10 ~~40~~. The compound of claim ~~39~~⁹, wherein R^{10} and R^{11} are each H and m = 2.

11 ~~41~~. The compound of claim ~~38~~⁵, wherein Z is Y_3C-O- and the groups Y are phenyl groups optionally substituted with one to two substituents selected from C_{1-3} alkoxy, C_{1-3} alkyl, halogen, OH, NO_2 , CN and $NR^{13}R^{14}$.

12 ~~42~~. The compound of claim ~~41~~, wherein the groups Y are identical and represent phenyl substituted with one C₁₋₃ alkoxy group.

13 ~~43~~. The compound of claim ~~42~~, wherein the phenyl groups are para-substituted with a C₁₋₂ alkoxy group.

14 ~~44~~. The compound of claim ~~41~~, wherein Z is Y₂C=CR¹⁵-, the groups Y are selected from optionally substituted phenyl and optionally substituted heteroaryl having 5 to 6 ring members and one to two heteroatoms independently selected from O, N and S and R¹⁵ is selected from H and CH₃.

15 ~~45~~. The compound of claim ~~44~~, wherein R¹⁵ is H.

16 ~~46~~. The compound of claim ~~45~~, wherein the groups Y carry 0, 1 or 2 substituents, the substituents being selected from C₁₋₃ alkyl, C₁₋₃ alkoxy, halogen, OH, NO₂, CN and NR¹³R¹⁴.

17 ~~47~~. The compound of claim ~~44~~, wherein the groups Y are the same and are selected from phenyl, 4-methoxyphenyl and 3-methyl-2-thienyl.

18 ~~48~~. The compound of claim ~~41~~, wherein Z is Y₂C=N-O- and the groups Y are selected from optionally substituted phenyl and optionally substituted heteroaryl having 5 to 6 ring members and one to two heteroatoms independently selected from O, N and S.

19 49. The compound of claim 41, wherein

R^1 to R^7 are independently selected from H, C_{1-3} alkyl and phenyl;

A^1 represents $(-CR^8R^9-)_n$, R^8 and R^9 are independently selected from H and C_{1-3} alkyl, and $n = 1$ or 2 ;

X is selected from COOM and groups which can be converted into COOM under physiological conditions, M being selected from H and Na;

A^2 is $(-CR^{10}R^{11}-)_m$, where R^{10} and R^{11} are independently selected from H and C_{1-2} alkyl and m is 2 or 3; and

Z is selected from Y_3C-O- and $Y_2C=CR^{15}-$, R^{15} is selected from H and methyl and the groups Y are identical and selected from optionally substituted C_{6-12} aryl and optionally substituted C_{2-5} heteroaryl having up to three heteroatoms independently selected from N, O and S.

20 50. The compound of claim 49, wherein R^1 to R^7 are independently selected from H and methyl.

21 51. The compound of claim 50, wherein R^8 and R^9 are independently selected from H and methyl, and $n = 1$.

22 52. The compound of claim 49, wherein R^{10} and R^{11} are independently selected from H and C_{1-2} alkyl and m is 2.

23 53. The compound of claim 52, wherein Z is Y_3C-O- and the groups Y are identical and

represent phenyl substituted with one C₁₋₃ alkoxy group.

24/ 54. The compound of claim 49, wherein Z is Y₂C=CH- and the groups Y are identical and selected from phenyl, 4-methoxyphenyl and 3-methyl-2-thienyl.

25/ 55. The compound of claim 49, wherein
R¹ to R⁷ are each H;
A¹ represents (-CR⁸R⁹-)_n, R⁸ and R⁹ are independently selected from H and methyl, and
n = 1 or 2;

X is COOM and M is selected from H and Na;

A² is (-CR¹⁰R¹¹-)_m, where R¹⁰ and R¹¹ are independently selected from H and methyl and m is 2; and

Z is Y₃C-O- and the groups Y are identical and selected from phenyl groups para-substituted with a C₁₋₂ alkoxy group.

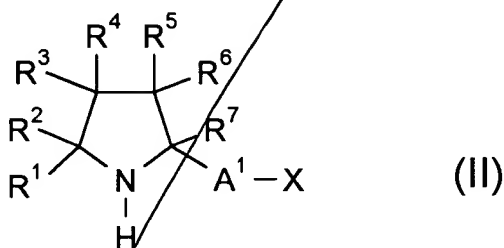
26/ 56. The compound of claim 49, wherein
R¹ to R⁷ are each H;
A¹ represents (-CR⁸R⁹-)_n, R⁸ and R⁹ are independently selected from H and methyl, and n = 1 or 2;

X is COOM and M is selected from H and Na;

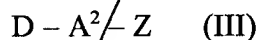
A² is (-CR¹⁰R¹¹-)_m, where R¹⁰ and R¹¹ are independently selected from H and methyl and m is 2; and

Z is $Y_2C=CH-$ and the groups Y are identical and selected from phenyl, 4-methoxyphenyl and 3-methyl-2-thienyl.

57. A process for the preparation of a compound of general formula (I) of claim 31, wherein a compound of general formula (II)



wherein R^1 to R^7 , A^1 and X are as defined in claim 31 is reacted with a compound of the general formula (III):

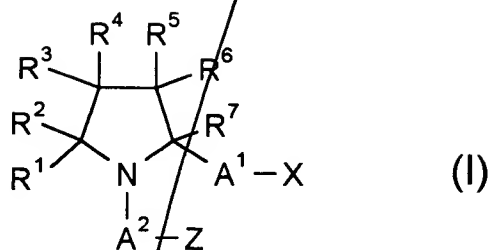


wherein A^2 and Z are defined as in claim 31 and D represents a group which can react with the group N-H of the compound of general formula (II) to form HD.

58. The process of claim 57, wherein D is halogen.

59. A pharmaceutical composition comprising at least one of a pharmaceutically acceptable carrier and a pharmaceutically acceptable excipient and at least one compound of general formula (I):

Sub C21



wherein

R^1 to R^7 are independently selected from H, optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl and C_{2-6} alkynyl, optionally substituted aryl or heteroaryl, OH, halogen, CN, OR^{12} , SR^{12} , COR^{12} , $COOR^{12}$, SOR^{12} , SO_2R^{12} , $NR^{13}R^{14}$, $CONR^{13}R^{14}$, $SO_2NR^{13}R^{14}$, where R^{13} and R^{14} are independently selected from H and C_{1-3} alkyl and R^{12} represents C_{1-6} alkyl; two of R^1 to R^7 , together with the atoms connecting them, each may form a 3- to 6-membered ring system, which ring system may contain one or more heteroatoms; R^1 and R^2 and/or R^3 and R^4 and/or R^5 and R^6 may be replaced by an optionally substituted alkylidene group or =O; and two of R^1 to R^7 which are positioned at adjacent carbon atoms may each be replaced by a C-C bond;

A^1 is selected from $(-CR^8R^9)_n$, optionally substituted C_{3-6} cycloalkylene and a combination of these groups, R^8 and R^9 being independently selected from H, C_{1-6} alkyl, halogen, OH, OR^{12} and $NR^{13}R^{14}$ and where for $n \geq 2$, R^8 and R^9 may be different in each group and two groups selected from R^8 and R^9 at adjacent C atoms may be replaced by a C-C bond, and a group -O- or -CO- may be positioned between two adjacent groups CR^8R^9 ; and wherein one of R^8 and R^9 may be combined with one of R^1 to R^7 to form a 5- to 7-membered ring structure; and $n = 0, 1, 2, 3$ or 4 ;

X is selected from COOM and groups which can be converted into COOM under physiological conditions, M being selected from H and pharmaceutically acceptable cations;

A^2 is $(-CR^{10}R^{11}-)_m$, where R^{10} and R^{11} are independently selected from H, C_{1-2} alkyl and halogen; where for $m \geq 2$ the groups R^{10} and R^{11} may be different in each group, a group -O- or -S- may be positioned between two adjacent groups $-CR^{10}R^{11}-$, and two groups selected from R^{10} and R^{11} at adjacent C atoms may be replaced by a C-C bond; and wherein one of R^{10} and R^{11} may be combined with one of R^1 to R^9 to form a 5- to 7-membered ring structure; and m is 1, 2, 3, or 4;

Z is selected from Y_3C-O- , $Y_2C=CR^{15}-$ and $Y_2C=N-O-$, where R^{15} is selected from H, C_{1-3} alkyl or halogen and the groups Y are independently selected from optionally substituted C_{6-12} aryl and optionally substituted C_{2-5} heteroaryl having up to three heteroatoms independently selected from N, O and S, and the groups Y may be linked by a covalent bond or by groups between atoms belonging to different groups Y, said groups selected from -O-, -S-, -NH-, -O-, -CH=CH-, -CH=N-, -CH₂- and -CH₂CH₂-;

28 ~~60~~. The pharmaceutical composition of claim ~~59~~, wherein

R^1 to R^7 are independently selected from H, C_{1-3} alkyl and phenyl;

A^1 represents $(-CR^8R^9-)_n$, R^8 and R^9 are independently selected from H and C_{1-3} alkyl, and $n = 1$ or 2 ;

X is selected from COOM and groups which can be converted into COOM under physiological conditions, M being selected from H and Na;

A^2 is $(-CR^{10}R^{11}-)_m$, where R^{10} and R^{11} are independently selected from H and C_{1-2} alkyl and m is 2 or 3; and


Z is selected from Y_3C-O- and $Y_2C=CR^{15}-$, R^{15} is selected from H and methyl and the groups Y are identical and selected from optionally substituted C_{6-12} aryl and optionally substituted C_{2-5}

heteroaryl having up to three heteroatoms independently selected from N, O and S.

29 ~~61~~. A method of treating a disease which can be one of ameliorated and cured by
amplification of GABAergic neurotransmission, the method comprising administering to a
patient in need of such treatment a compound of claim ~~31~~ in an amount sufficient to ameliorate or
cure the disease.---

Should there be any questions, the Examiner is invited to contact the undersigned at the
below-listed telephone number.

Respectfully submitted,
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